

AMENDMENTS

A Version With Markings to Show Changes Made follows Applicant's Remarks beginning at page 14.

In the Claims:

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Please cancel Claims 3, 6, 13, 14 and 15, without prejudice. Please amend Claims 1, 5, 11, 16, 17, 21, 22, 23 and 25 as follows.

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1. (Twice Amended) An in vitro method of transdifferentiating an epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, comprising:
- (a) culturing a proliferating epidermal basal cell population comprising one or more epidermal basal cell(s), said cell(s) derived from the skin of a mammalian subject;
 - (b) transfecting said epidermal basal cell, in vitro, with one or more eukaryotic expression vector(s) containing at least one cDNA encoding a human neurogenic transcription factor, or homologous non-human counterpart, or active fragment(s) thereof, selected from the group consisting of NeuroD1, NeuroD2, ASH1, Zic1, Zic3, and MyT1, such that at least one of the neurogenic transcription factor(s) is expressed in said cell;
 - (c) growing the transfected cell in the presence of at least one antisense oligonucleotide comprising a segment of a human MSX1 gene and/or human HES1 gene, or homologous non-human counterpart of either of these, in an amount sufficient to suppress the expression of functional MSX1 gene product and/or HES1 gene product;
 - (d) growing said epidermal cell with a retinoid and at least one [neurotrophin] signal molecule selected from the group consisting of BDNF, CNTF, PDGF, NGF, NT-3, NT-4, sonic

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hedgehog, and sonic hedgehog aminoterminal peptide, or a cytokine comprising IL-6, whereby the cell is transdifferentiated into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell; and

(e) wherein the physiological and/or immunological feature is expression of a marker selected from the group consisting of nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2, glial fibrillary acidic protein (GFAP), O4, or a combination of any of these.

2. (Reiterated) The method of Claim 1, wherein the eukaryotic expression vector(s) of the transfection step comprise a CMV promoter sequence operatively linked to a DNA(s) encoding the neurogenic transcription factor selected from the group consisting of NeuroD1, NeuroD2, ASH1, Zic1, Zic3, and MyT1, and wherein the DNA encoding the neurogenic transcription factor is of human origin or is a homologous non-human counterpart, or is an active fragment of a gene encoding any of these.

3. Canceled.

4. (Reiterated) The method of Claim 1, wherein the morphological feature comprises one or more morphological neurite-like process(es) at least about 50 micrometers in length.

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5. (Amended) A transdifferentiated cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, comprising:

an epidermal basal cell transfected with one or more expression vectors comprising a CMV promoter sequence operatively linked to a DNA(s) encoding the neurogenic transcription factor NeuroD1, NeuroD2, ASH1, Zic1, Zic3, or MyT1, wherein the DNA encoding the neurogenic transcription factor is of human origin, or is a non-human homologous counterpart, or is an active fragment of a gene encoding any of these, said cell being treated with at least one

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antisense oligonucleotide comprising a segment(s) of human MSX1 gene or human HES1 gene, or non-human homologous counterpart thereof, and wherein said cell was grown in the presence of a retinoid and at least one signal molecule selected from the group consisting of BDNF, CNTF, NGF, NT-3, NT-4, IL-6, sonic hedgehog, and sonic hedgehog aminoterminal peptide, thereby transdifferentiating said epidermal basal cell into a cell having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell said cell expressing at least one marker selected from the group consisting of nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2, glial fibrillary acidic protein (GFAP), O4, or a combination of any of these.

6. Canceled.

7. (Reiterated) The transdifferentiated cell of Claim 5, wherein the morphological feature comprises one or more morphological neurite-like process(es) at least about 50 micrometers in length.

8. (Reiterated) A transdifferentiated cell produced by the process of Claim 1.

9. (Reiterated) The transdifferentiated cell of Claim 8, wherein the physiological and/or immunological feature expressed by the cell is a marker selected from the group consisting of nestin, neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2, glial fibrillary acidic protein (GFAP), O4, or a combination of any of these.

10. (Reiterated) The transdifferentiated cell of Claim 8, wherein the morphological feature expressed by the cell is one or more morphological neurite-like process(es) at least about 50 micrometers in length.

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11. (Twice Amended) A kit for converting, in vitro, epidermal basal cells into cells having one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell, said kit comprising:

(a) one or more eukaryotic expression vector(s) containing cDNA encoding a neurogenic transcription factor, or fragment thereof, from the group consisting of NeuroD1, NeuroD2, ASH1, Zic1, Zic3, and MyT1, or a non-human homologous counterpart of any of these;

(b) at least one antisense oligonucleotide corresponding to the human MSX1 gene, the human HES1 gene, or a non-human homologous counterpart of either of these; and

(c) a retinoid and at least one signal molecule selected from the group consisting of BDNF, CNTF, PDGF, NGF, NT-3, NT-4, sonic hedgehog, and sonic hedgehog aminoterminal peptide.

12. (Reiterated) The kit of Claim 11, further comprising instructions for using (A), (B), and (C) in transdifferentiating a mammalian subject's epidermal basal cell(s).

13. Canceled.

14. Canceled.

15. Canceled.

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16. (Amended) The transdifferentiated cell of Claim 8, wherein the cell further displays the physiological feature of a lack of mitotic activity under cell culture conditions which induce differentiation in neural progenitor cells.

17. (Amended) The cell of Claim 8, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to a neuronal cell.

18. (Reiterated) The transdifferentiated cell of Claim 17, wherein the physiological and/or immunological feature is expression of neural RNA-binding protein Musashi, neurofilament M, neural-specific β -tubulin, neural-specific enolase, microtubule associated protein 2.

19. (Reiterated) The transdifferentiated cell of Claim 17, wherein the cell is a GABAergic cell.

20. (Reiterated) The transdifferentiated cell of Claim 17, wherein the cell is a dopaminergic cell.

21. (Amended) The transdifferentiated cell of Claim 8, wherein the morphological feature is one or more neurite-like process(es) at least about 50 micrometers in length.

22. (Amended) The transdifferentiated cell of Claim 8, wherein the cell is of human origin.

23. (Amended) The cell of Claim 8, wherein the transdifferentiated cell has a morphological, physiological, or immunological feature specific to an astroglial or oligodendroglial cell.

24. (Reiterated) The transdifferentiated cell of Claim 23, wherein the physiological and/or immunological feature is expression of glial fibrillary acidic protein (GFAP) or O4.

25. (Amended) An in vitro cell culture derived from the transdifferentiated cell of Claim 8, comprising a plurality of cells that express one or more morphological, physiological and/or immunological feature(s) of a neural progenitor, neuronal, or glial cell.